

AMENDMENTS TO THE SPECIFICATION

(Amendments are illustrated by showing deletions ~~by strikethrough~~ and additions by underlining)

The following application page references correspond to the publication of the international application PCTUS00/17401 (WO 01/00676), from which the present national filing is based.

1. Below the Title of the Application and before the Background of the Invention, please insert the following new paragraph:

--Cross Reference to Related Applications

This application is a United States national filing under 35 U.S.C. §371 of international (PCT) application No.

PCT/US00/17401, filed June 23, 2000, designating the US, and claiming priority to United States provisional application serial number 60/141,028, filed June 25, 1999.--

2. Please amend page 2, the first full paragraph, to appear as follows:

--The peptides of formula (I) are a sub-genus encompassed by a genus of compounds described and claimed in ~~pending~~ U.S. Application No. 08/855,204, filed May 13, 1997, now U.S. Patent No. 6,262,229, issued July 17, 2001 ~~which application is~~ and assigned in part to the assignee of the present invention. The compounds of formula (I) of the present application are not specifically described in U.S. ~~Application Patent No. 08/855,204 6,262,229~~. It has been unexpectedly and surprisingly discovered that the compounds of formula (I) of the present invention possess somatostatin agonist activity. This is an unexpected and surprising discovery since the compounds of U.S. ~~Application Patent No. 08/855,204 6,262,229~~ were originally found to possess somatostatin antagonist activity.--

3. Please amend the paragraph spanning pages 13 through 15 to appear as follows:

-- As is well known to those skilled in the art, the known and potential uses of somatostatin are varied and multitudinous. Thus, the administration of a peptide of this invention for purposes of stimulating the somatostatin receptors can have the same effects or uses as somatostatin itself. For example, inhibiting the secretion of growth hormone, insulin, glucagon and pancreatic exocrine secretion (U.S. Patent No. 4,853,371); for treating restenosis (U.S. Patent No. 5,147,856); for treating hepatoma (U.S. Patent No. 5,411,943); for treating lung cancer (U.S. Patent No. 5,073,541); treating melanoma (U.S. Patent No. 6,087,337 issued July 11, 2000 Application No. 08/089,410 filed July 9, 1993); for inhibiting the accelerated growth of a solid tumor (U.S. Patent No. 5,504,069); for decreasing body weight (U.S. Application No. 08/854,941 filed May 13, 1997); for treating insulin resistance and Syndrome X (U.S. Application No. 08/854,943 filed May 13, 1997); for prolonging the survival of pancreatic cells (U.S. Patent No. 5,688,418); for treating fibrosis (PCT Application No. PCT/US97/14154); for treating hyperlipidemia (U.S. Application No. 08/855,311 filed May 13, 1997); for treating hyperamylinemia (U.S. Patent No. 5,763,200 issued June 9, 1998 Application No. 08/440,061 filed May 12, 1995); for treating hyperprolactinemia and prolactinomas (U.S. Patent No. 5,972,893 issued October 26, 1999 Application No. 08/852,221 filed May 7, 1997); Cushings Syndrome (see Clark, R.V. et al, Clin. Res. 38, p. 943A, 1990); gonadotropinoma (see Ambrosi B., et al., Acta Endocr. (Copenh.) 122, 569-576, 1990); hyperparathyroidism (see Miller, D., et al., Canad. Med. Ass. J., Vol. 145, pp. 227-228, 1991); Paget's disease (see, Palmieri, G.M.A., et al., J. of Bone and Mineral Research, 7, (Suppl. 1), p. S240 (Abs. 591), 1992); VIPoma (see Koberstein, B., et al., Z.

Gastroenterology, 28, 295-301, 1990 and Christensen, C., *Acta Chir. Scand.* 155, 541-543, 1989); nesidioblastosis and hyperinsulinism (see Laron, Z., *Israel J. Med. Sci.*, 26, No. 1, 1-2, 1990, Wilson, D.C., *Irish J. Med. Sci.*, 158, No. 1, 31-32, 1989 and Micic, D., et al., *Digestion*, 16, Suppl. 1.70. Abs. 193, 1990); gastrinoma (see Bauer, F.E., et al., *Europ. J. Pharmacol.*, 183, 55 1990); Zollinger-Ellison Syndrome (see Mozell, E., et al., *Surg. Gynec. Obstet.*, 170, 476-484, 1990); hypersecretory diarrhea related to AIDS and other conditions (due to AIDS, see Cello, J.P., et al., *Gastroenterology*, 98, No. 5, Part 2, Suppl., A163 1990; due to elevated gastrin-releasing peptide, see Alhindawi, R., et al., *Can. J. Surg.*, 33, 139-142, 1990; secondary to intestinal graft vs. host disease, see Bianco J.A., et al., *Transplantation*, 49, 1194-1195, 1990; diarrhea associated with chemotherapy, see Petrelli, N., et al., *Proc. Amer. Soc. Clin. Oncol.*, Vol. 10, P 138, Abstr. No. 417 1991); irritable bowel syndrome (see O'Donnell, L.J.D., et al., *Aliment. Pharmacol. Therap.*, Vol. 4., 177-181, 1990); pancreatitis (see Tulassay, Z., et al., *Gastroenterology*, 98, No. 5, Part 2, Suppl., A238, 1990); Crohn's Disease (see Fedorak, R.N., et al., *Can. J. Gastroenterology*, 3, No. 2, 53-57, 1989); systemic sclerosis (see Soudah, H., et al., *Gastroenterology*, 98, No. 5, Part 2, Suppl., A129, 1990); thyroid cancer (see Modigliani, E., et al., *Ann. Endocr. (Paris)*, 50, 483-488, 1989); psoriasis (see Camisa, C., et al., *Cleveland Clinic J. Med.*, 57, No. 1, 71-76, 1990); hypotension (see Hoeldtke, R.D., et al., *Arch. Phys. Med. Rehabil.*, 69, 895-898, 1988 and Kooner, J.S., et al., *Brit. J. Clin. Pharmacol.*, 28, 735P-736P, 1989); panic attacks (see Abelson, J.L., et al., *Clin. Psychopharmacol.*, 10, 128-132, 1990); sclerodoma (see Soudah, H., et al., *Clin. Res.*, Vol. 39, p. 303A, 1991); small bowel obstruction (see Nott, D.M., et al., *Brit. J. Surg.*, Vol. 77, p. A691, 1990); gastroesophageal reflux (see Branch, M.S., et al., *Gastroenterology*, Vol. 100, No. 5, Part 2 Suppl., p. A425, 1991); duodenogastric reflux (see Hasler,

W., et al., *Gastroenterology*, Vol. 100, No. 5, Part 2, Suppl., p. A448, 1991); Graves' Disease (see Chang, T.C., et al., *Brit. Med. J.*, 304, p. 158, 1992); polycystic ovary disease (see Prelevic, G.M., et al., *Metabolism Clinical and Experimental*, 41, Suppl. 2, pp 76-79, 1992); upper gastrointestinal bleeding (see Jenkins, S.A., et al., *Gut.*, 33, pp. 404-407, 1992 and Arrigoni, A., et al., *American Journal of Gastroenterology*, 87, p. 1311, (abs. 275), 1992); pancreatic pseudocysts and ascites (see Hartley, J.E., et al.; *J. Roy. Soc. Med.*, 85, pp. 107-108, 1992); leukemia (see Santini, et al., 78, (Suppl. 1), p. 429A (Abs. 1708), 1991); meningioma (see Koper, J.W., et al., *J. Clin. Endocr. Metab.*, 74, pp. 543-547, 1992); and cancer cachexia (see Bartlett, D.L., et al., *Surg. Forum.*, 42, pp. 14-16, 1991).--

4. Please amend page 17, the first full paragraph to appear as follows:

--Further, a compound of this invention can be administered in a sustained release composition such as those described in the following patents and patent applications. U.S. Patent No. 5,672,659 teaches sustained release compositions comprising a bioactive agent and a polyester. U.S. Patent No. 5,595,760 teaches sustained release compositions comprising a bioactive agent in a gelable form. U.S. Patent No. 5,821,221, teaches polymeric sustained release compositions comprising a bioactive agent and chitosan. U.S. Patent No. 5,916,883, issued June 26, 1999 Application No. 08/740,778 filed November 1, 1996, teaches sustained release compositions comprising a bioactive agent and cyclodextrin. U.S. Application No. 09/015,394 filed January 29, 1998, teaches absorbable sustained release compositions of a bioactive agent. U.S. Application No. 09/121,653 filed July 23, 1998, teaches a process for making microparticles comprising a therapeutic agent such as a peptide in an oil-in-water process. U.S. Application No. 09/131,472 filed August 10, 1998, teaches